

FIGURE 1A

Human G Protein Coupled Receptor Family

(Receptors known as of January, 1999)

CLASS	LIGAND	NUMBER	TISSUE	PHYSIOLOGY	THERAPEUTICS
•Class I Rhodopsin like					
	•Amine				
	•Acetylcholine (muscarinic & nicotinic)	5	Brain, Nerves, Heart	Neurotransmitter	Acuity, Alzheimer's
	•Adrenoceptors				
	•Alpha Adrenoceptors	6	Brain, Kidney, Lung	Gluconeogenesis	Diabetes, Cardiovascular
	•Beta Adrenoceptors	3	Kidney, Heart	Muscle Contraction	Cardiovascular, Respiratory
	•Dopamine	5	Brain, Kidney, GI	Neurotransmitter	Cardiovascular, Parkinson's
	•Histamine	2	Vascular, Heart, Brain	Vascular Permeability	Anti-inflammatory, Ulcers
	•Serotonin (5-HT)	16	Most Tissues	Neurotransmitter	Depression, Insomnia, Analgesic
	•Peptide				
	•Angiotensin	2	Vascular, Liver, Kidney	Vasoconstriction	Cardiovascular, Endocrine
	•Bradykinin	1	Liver, Blood	Vasodilation,	Anti-inflammatory, Asthma
	•C5a anaphylatoxin	1	Blood	Immune System	Anti-inflammatory
	•Fmet-leu-phe	3	Blood	Chemoattractant	Anti-inflammatory
	•Interleukin-8	1	Blood	Chemoattractant	Anti-inflammatory
	•Chemokine	6	Blood	Chemoattractant	Anti-inflammatory
	•Orexin	2	Brain	Fat Metabolism	Obesity
	•Nociceptin	1	Brain	Bronchodilator, Pain	Airway Diseases, Anesthetic
	•CCK (Gastrin)	2	Gastrointestinal	Motility, Fat Absorption	Gastrointestinal, Obesity, Parkinson's
	•Endothelin	2	Heart, Bronchus, Brain	Muscle Contraction	Cardiovascular, Respiratory
	•Melanocortin	5	Kidney, Brain	Metabolic Regulation	Anti-inflammatory, Analgesics
	•Neuropeptide Y	5	Nerves, Intestine, Blood	Neurotransmitter	Behavior, Memory, Cardiovascular
	•Neurotensin	1	Brain,	CNS	Cardiovascular, Analgesic
	•Opioid	3	Brain,	CNS	Depression, Analgesic
	•Somatostatin	5	Brain, Gastrointestinal	Neurotransmitter	Oncology, Alzheimer's
	•Tachykinin (Substance P, NKA ₁)	3	Brain Nerves	Neurohormone	Depression, Analgesic



REPLACEMENT SHEET



REPLACEMENT SHEET

FIGURE 1B

•Thrombin	3	Platelets, Blood Vessels	Coagulation	Anti-coagulant, Anti-inflammatory
•Vasopressin-like	4	Arteries, Heart, Bladder	Water Balance	Anti-diuretic, Diabetic Complications
•Galanin	1	Brain, Pancreas	Neurotransmitter	Analgesics, Alzheimer's
•Hormone protein				
•Follicle stimulating hormone	1	Ovary, Testis	Endocrine	Infertility
•Lutropin-choriogonadotropic	1	Ovary, Testis	Endocrine	Infertility
•Thyrotropin	1	Thyroid	Endocrine	Thyroidism, Metabolism
•(Rhod)opsin				
•Opsin	5	Eye	Photoreception	Ophthalmic Diseases
•Olfactory	4(~1000)	Nose	Smell	Olfactory Diseases
•Prostanoid				
•Prostaglandin	5	Arterial, Gastrointestinal	Vasodilation, Pain	Cardiovascular, Analgesic
•Lysophosphatidic Acid	2	Vessels, Heart, Lung	Inflammation	Cancer, Anti-Inflammatory
•Sphingosine-1-phosphate	2	Most Cells	Cell proliferation	Cancer
•Leukotriene	1	White Blood Cells, Bronchus	Inflammation	Asthma, Rheumatoid Arthritis
•Prostacyclin	1	Arterial, Gastrointestinal	Platelet Regulation	Cardiovascular
•Thromboxane	1	Arterial, Bronchus	Vasoconstriction	Cardiovascular, Respiratory
•Nucleotide-like				
•Adenosine	4	Vascular, Bronchus	Multiple Effects	Cardiovascular, Respiratory
•Purinocceptors	4	Vascular, Platelets	Relaxes Muscle	Cardiovascular, Respiratory
•Cannabis	2	Brain	Sensory Perception	Analgesics, Memory
•Platelet activating factor	1	Most Peripheral Tissues	Inflammation	Anti-inflammatory, Anti-asthmatic
•Gonadotropin-releasing hormone like				
•Gonadotropin-releasing hormone	1	Reproductive Organs, Pituitary	Reproduction	Prostate Cancer, Endometriosis
•Thyrotropin-releasing hormone	1	Pituitary, Brain	Thyroid Regulation	Metabolic Regulation
•Growth hormone-inhibiting factor	1	Gastrointestinal	Neuroendocrine	Oncology, Alzheimer's
•Melatonin	1	Brain, Eye, Pituitary	Neuroendocrine	Regulation of Circadian Cycle
•Secretin	1	Gastrointestinal, Heart	Digestion	Obesity, Gastrointestinal
•Calcitonin	1	Bone, Brain	Calcium Resorption	Osteoporosis
•Corticotropin releasing factor/urocortin	1	Adrenal, Vascular, Brain	Neuroendocrine	Stress, Mood, Obesity
•Gastric inhibitory peptide (GIP)	1	Adrenals, Fat Cells	Sugar/Fat Metabolism	Diabetes, Obesity
•Glucagon	1	Liver, Fat Cells, Heart	Gluconeogenesis	Cardiovascular

•Class II
Secretin like



REPLACEMENT SHEET

FIGURE 1C

•Glucagon-like Peptide 1 (GLP-1)	1	Pancreas, Stomach, Lung	Gluconeogenesis	Cardiovascular, Diabetes, Obesity
•Growth hormone-releasing hormone	1	Brain	Neuroendocrine	Growth Regulation
•Parathyroid hormone	1	Bone, Kidney	Calcium Regulation	Osteoporosis
•PACAP	1	Brain, Pancreas, Adrenals	Metabolism	Metabolic Regulation
•Vasoactive intestinal polypeptide (VIP)	1	Gastrointestinal	Motility	Gastrointestinal
•Metabotropic Glutamate	7	Brain	Sensory Perception	Hearing, Vision
•GABA _B	1	Brain	Neurotransmitter	Mood Disorders
•Extracellular Calcium Sensing	1	Parathyroid, Kidney, GI Tract	Calcium Regulation	Cataracts, GI Tumors

•Class III



REPLACEMENT SHEET
FIGURE 2A

G protein-coupled receptors:
(Division into Class A
Or Class B)

1. **A1 adenosine receptor** [Homo sapiens]. ACCESSION AAB25533
npivyaf riqkfrvtfl kiwndhfrq pappidedlp eerpdd
Class A
2. **adrenergic, alpha -1B-, receptor** [Homo sapiens]. ACCESSION NP_000670
npiiypc sskefkrafv rilgcqcrgr grmmrrrr lggcaytyrp wtrggslers qsrkdsldds gscslgsqrt
lpsaspspgy lgrgappve lcafpewkap gallslpape ppgrgrhds gplftfkllt epespqtdgg asnggceaaa
dvangqpgfk snmplapgqf
Class A
3. **adrenergic receptor alpha-2A** [Homo sapiens]. ACCESSION AAG00447
npviytifn hdfrrafkki lergdrkriv
Class A
4. **alpha-2B-adrenergic receptor - human.** ACCESSION A37223
npviytifn qdfrrafri lcrpwtqtaw
Class A
5. **alpha-2C-adrenergic receptor - human.** ACCESSION A31237
npviytfvn qdfrrsfkhi lfrmrgrf q
Class A
6. **beta-1-adrenergic receptor** [Homo sapiens]. ACCESSION NP_000675
npiiycrs pdfrkafqgl lccarraarr rhathgdrpr asgclarpgp ppspgaasdd ddddvvgatp parllepwag
cnggaaadsd ssldepcrpg faseskv
Class A
7. **beta-2 adrenergic receptor.** ACCESSION P07550
npliyrcrsp dfriaqell clrrsslkay gngyssngnt 361 geqsgyhveq ekenklced lpgtedfvgh qgtvpsdnid
sqgrncstnd sll
Class A
8. **dopamine receptor D1** [Homo sapiens]. ACCESSION NP_000785
npii yafnadfrka fstllgcyr lcpatnnaiet vsinnngaam fsshheprgs iskecnlvyl iphavgsedd
lkkeeaagia rpleklspal svildytdv slekiqpitiq ngqhpt
Class A
9. **D(2) dopamine receptor.** ACCESSION P14416
npiiyttfn iefrkafiki lhc
Class A



REPLACEMENT SHEET

FIGURE 2B

10. **d3 dopamine receptor - human. ACCESSION G01977**
np viyttfnief rkafkilsce
Class A
11. **dopamine receptor D4 - human. ACCESSION DYHUD4**
npviyvtv fnaefrnfvr kalracc
Class A
12. **dopamine receptor D5 - human. ACCESSION DYHUD5**
npviya fnadfqkvfa qllgcshfcs rtpvetvnis nelisynqdi vfhkeiaaay ihmmpnavtp gnrevdndee
egpfdrmfqi yqtspdgdpv aesvweldec geislckitp ftpngfh
Class A
13. **muscarinic acetylcholine receptor M1 [Homo sapiens]. ACCESSION NP_000729**
nrmcyal cnkafdrtdfr llllcrwdkr rwrkipkrpg svhrtpsrgc
Class A
14. **muscarinic acetylcholine receptor M2 [Homo sapiens]. ACCESSION NP_000730**
npacy alcnatfkkt fkhllmchyk nigatr
Class A
15. **muscarinic acetylcholine receptor M3 [Homo sapiens]. ACCESSION NP_000731**
n pveyalenkt frttfkmlll cqcdkkkrrk qqyqqrsqi fhkrapeqal
Class A
16. **muscarinic acetylcholine receptor M4 [Homo sapiens]. ACCESSION NP_000732**
npa cyalcnatfk ktrfhlllcq yrnigtar
Class A
17. **m5 muscarinic receptor. locus HUMACHRM ACCESSION AAA51569**
npicyalcnr tfrktfkml lcrwkkkkve eklywqgnsk lp
Class A
18. **5-hydroxytryptamine (serotonin) receptor 1A [Homo sapiens]. ACCESSION BAA90449**
npviy ayfnkdfqna fkkiikckf
Class A
19. **5-hydroxytryptamine (serotonin) receptor 1B [Homo sapiens]. ACCESSION BAA94455**
npiiyt msnedfkqaf hklirfkcts
Class A
20. **5-hydroxytryptamine (serotonin) receptor 1E [Homo sapiens]. ACCESSION BAA94458**
n pllytsfnd fklafkkliir cre
Class A

REPLACEMENT SHEET

FIGURE 2C



21. **OLFACTORY RECEPTOR 6A1. ACCESSION O95222**
npiiyclmq evkralccil hlyqhdpdp kkgsmv
Class A
22. **OLFACTORY RECEPTOR 2C1. ACCESSION O95371**
npliy tlrmmevkga lrrllgkgre vg
Class A
23. **angiotensin receptor 1 [Homo sapiens]. ACCESSION NP_033611**
npl fyglgkfk ryflqllyi ppkakshnl sfkmsflsy psdnvssstk kpapcfeve
Class B
24. **angiotensin receptor 2 [Homo sapiens]. ACCESSION NP_000677**
npflycf vgnrfqqklr svfrvpitwl qgkresmscr kssslremet fvs
Class B
25. **interleukin 8 receptor beta (CXCR2) [Homo sapiens]. ACCESSION NM_001557**
NPLIYAFIGQKFRHGLLKILAIHGLISKDSLPKDSRPSFVGSSSGHTSTTL
Class B
26. **cx3c chemokine receptor 1 (cx3cr1) (fractalkine receptor)**
ACCESSION P49238
np liyafagekf rrylyhlygk clavlgrsv hvdffsssesq rsrhgsvlss nftyhtsdgd alll
Class B
27. **neurotensin receptor - human. ACCESSION S29506**
n pilynlvsan frhiflatla clcpvwrrr krpafsrkad svssnhflss natretly
Class B
28. **SUBSTANCE-P RECEPTOR (SPR) (NK-1 RECEPTOR) (NK-1R). ACCESSION P25103**
npiyyccldn rrlglfkhafrccpfisagd yeglemkstr ylqtqgsvyk vsrletfistvgaheeepe dgpkatpssl
dltsncssrs dsktmtesfs fssnvl
Class B
29. **vasopressin receptor type 2 [Homo sapiens]. ACCESSION AAD16444**
npwiyasfss svsselrll ccargtrpps lgpqdescft asslakdts s
Class B
30. **thyrotropin-releasing hormone receptor - human. ACCESSION JN0708**
npviy nlmsqkfraa frklenckqk ptepanysv alnysvikes dhfstelddi tvtdtylsaf kvsfddtcla sevsvfsqs
Class B
31. **oxytocin receptor - human. ACCESSION A55493**
npwiy lftghlfhel vqrfccsas ylkgrlget saskksnsss fvlshrsss q rscsqpsta
Class B

REPLACEMENT SHEET

FIGURE 2D



32. **neuromedin U receptor [Homo sapiens].** ACCESSION AAG24793
npvlyslmssrfretfqaclcgacchrlrprhsshslsrmttgstlcvdvgslgswvhplagndgpeaqgetdps
Class B
33. **gastrin receptor.** ACCESSION AAC37528
nplvy cfmhrrfrqa cletcarccp rpprarpral pdedpptpsi aslsrlytt isflgpg
Class B
34. **galanin receptor 3 [Homo sapiens].** ACCESSION 10879541
nplv yalashrfra rfrlwpcgr rrrharral rrvrpassgp pgcpgdarps grllagggqg pepregpvhg geaargpe
Class A
35. **edg-1 - human.** ACCESSION A35300
npiiy tltnkemrra firimsceck psqdsagkfk rpiiagmefs rksdnsshp 361 qkdegdnpet imssgnvnss s
Class A
36. **central cannabinoid receptor [Homo sapiens].** ACCESSION NP_057167
npiiyalr skdlrhafns mfpscegtaq pldnsmgdsd clkhannaa svhraesci kstvkiaqvt msvstdtsae al
Class A
37. **delta opioid receptor - human.** ACCESSION I38532
npvlyaf ldenfkrcfr qlcrkpcgrp dpssfsrpre atarervtac tpsdpggggr aa
Class A
38. **proteinase activated receptor 2 (PAR-2) human.** ACCESSION P55085
dpfvyyfvshdfrdhaknallersvrtvkqmqvsltskkhsrksssysssttvktsy
Class A
39. **vasopressive intestinal peptide receptor (VIPR) rat.** ACCESSION NM_012685
NGEVQAELRRKWRRWHLQGVLGWSSKSQHPWGGSNGATCSTQVSMLTRVSPSARR
SSSFQAEVSLV
Class B

REPLACEMENT SHEET



FIGURE 3A

Human V2R DNA (nucleotides encoding the last 29 amino acids of the V2R and the adjacent stop codon):

**gcccggggacgcacccccaccagcctgggtccccaagatgagtctgcaccaccgccagtcct
ccctggccaaggacattcatcgtga**

FIGURE 3B

PCR amplified human V2R DNA fragment:

**gcggccgcacggggacgcacccccaccagcctgggtccccaagatgagtctgcaccaccgcc
agctcctccctggccaaggacattcatcgtgaagatctccgcggtctaga**

*Additions and changes to the V2R DNA are underlined.

*The Sma I (cccggg) restriction enzyme site (underlined in Fig. 3A) was eliminated in the amplified DNA fragment by changing a cytosine to an adenine.

*A Not I restriction site (gcggccgc) was incorporated into the amplified DNA fragment by adding 6 nucleotides (gcggcc) to the 5' end of the V2R DNA.

*Bgl II (agatct), Sac II (ccgcgg), and Xba I (tctaga) restriction enzyme sites were added to the 3' end of the V2R DNA.

REPLACEMENT SHEET

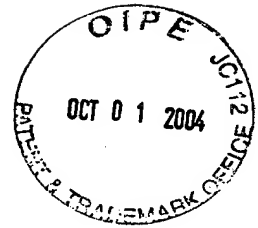


FIGURE 4A

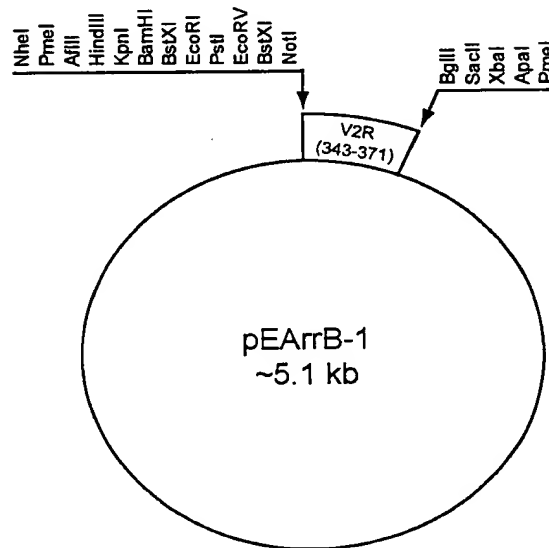


FIGURE 4B

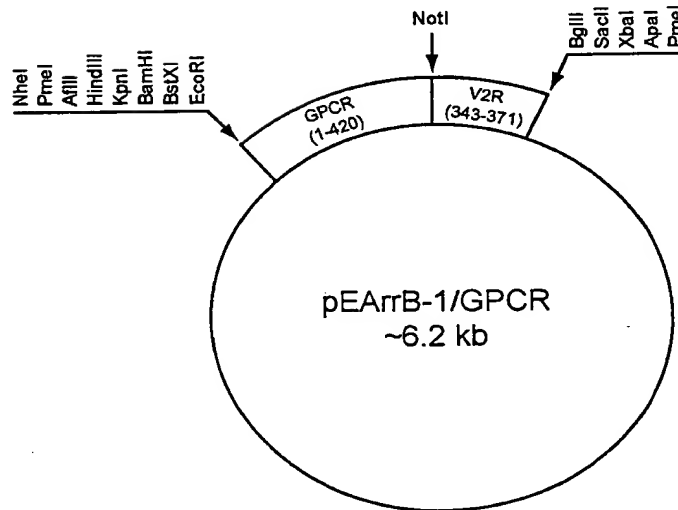


FIGURE 4C

...AAARGRTPPSLGPQDESCCTASSSLAKDTSS

REPLACEMENT SHEET



FIGURE 7B

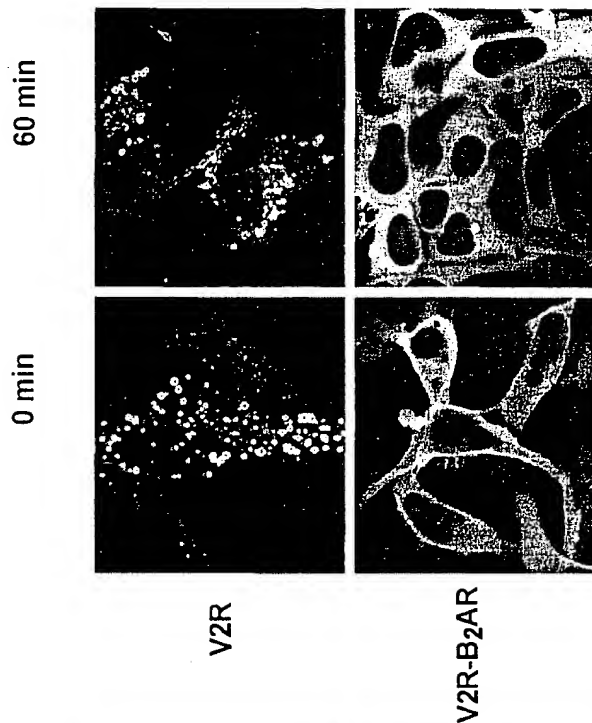
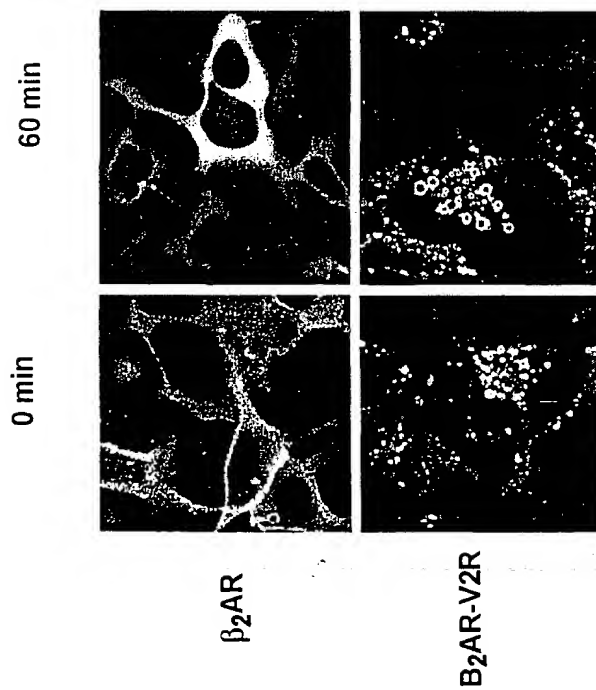


FIGURE 7A



REPLACEMENT SHEET



FIGURE 8A

1) V2R	CARGRTPPSLGPDSCCTTASSSLAKDTSS
2) V2R-S362X	CARGRTPPSLGPDSCCTTA
3) V2R-SSSTSS/AAAAAA	CARGRTPPSLGPDSCCTTAAAAALAKDAAA
4) V2R-TSS/AAA	CARGRTPPSLGPDSCCTTASSSLAKDAAA
5) V24-SSS/AAA	CARGRTPPSLGPDSCCTTAAAAALAKDTSS
6) β_2 AR-V2R-SSS/AAA	CARGRTPPSLGPDSCCTTAAAAALAKDTSS
7) β_2 AR	CLRRSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLCEDLP- GTEDFVGHQGTVPDNDIDSQGRNCSTNDSSL
8) β_2 AR413-V2R10	CLRRSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLCEDLP- GTEDFVGHQGTVPDNDIDSQGRNCSTNDSSLSSSLAKDTSS
9) β_2 AR360-V2R10	CLRRSSLKAYGNGYSSNGNTSSSLAKDTSS

FIGURE 8B

V2R	NPWIYASFSSSVSSELRSLLCCARGRTPPSLGPDSCCTTASSSLAKDTSS
AAA-1	-----AAA-----
AAA-2	-----AAA-----
NTR-1	NPILYNLVSANFRQVFLSTLACLCPGWRHRRKKRPTFSRKPNSSSNHAFSTSATRETL
AMAA	-----A-AA-----
AAA	-----AAA-----
OTR	NPWIYMLFTGHLFHELVRFLCCSASYLKGRRLGETSASKKSNSSSFVLSHRSSQRSCSQPSTA
AAAA	-----AAAA-----
AAA-1	-----AAA-----
AAA-2	-----AAA-----

FIGURE 8C

REPLACEMENT SHEET



SPR	NPIIYCCINDRFRLGFKHAFRCCPFISAGDYEGLMKSTRYLQTOGVYKVSRLTTISTVVGAAHEEPEDEGPKATPSSLKLTISNCSSRSDSKIMTESF'SFSSNVLS
383X	-----X
355X	-----X
325X	-----X
AAIAA	-----AA-AA
APAA	-----A-AA

REPLACEMENT SHEET



FIGURE 9A

Amino Acid Sequence of the Wild-Type Receptors

Amino acid sequence of the wild-type V2R

MLMASTTSAPVPGHPSLPSLPSNSSQERPLDTRDPLLARAELALLSIVFVAVALSNGLVLAA
LARRGRRGHWAPIHVFIGHLCLADLAVALFQVLPQLAWKATDRFRGPDALCRAVKYLQMVG
MYASSYMILAMTLDRHRAICRPMLAYRHGSGAHWNRPVLVAWAFSLLLSLPQLFIFAQRNV
EGSGVTDWCWACFAEPWGRRTYVTWIALMVFVAPTGLGIAACQVLIFREIHASLVPGPSE
GRRRRGRRTGSPGEGAHVSAAVAKTVRMTLVIVVVVLCWAPFFLVQLWAAWDPEAPLEGA
PFVLLMLLASLNSCTNPWIIYASFSSSVSSELRSLLCCARGRTPPSLGPQDESCTTASSSLA
KDTSS

(Seq. ID No. 1)

FIGURE 9B

Amino acid sequence of the wild-type β_2 AR

MGQPGNGSAFLLAPNRSHAPDHDVTQQRDEVWVVGMGIVMSLIVLAIVFGNVLVITAIK
ERLQTVTNFYFITSACADLVMGAVVPFGAAHILMKMWTFGNFWCEFWTSIDVLCVTASIE
TLCVIAVDYFAITSPFKYQSLLTKNKARVILMVWIVSGLTSFLPIQMHWRATHQEAIN
CYANETCCDFFTQAYAIASSIVSFYVPLVIMVFVYSRVFQEAQRQLQKIDKSEGRFHVQN
LSQVEQDGRGTGHGLRRSSKFCLKEHKALKTLGIIMGTFTLCWLPFFIVNIVHVIQDNLIRK
EVYILLNWIGYVNSGFNPLIYCRSPDFRIAFQELLCLRRSSLKAYGNGYSSNGNTGEQSGY
HVEQEKENKLLCEDLPGTEDFVGHQGTVPDNDISQGRNCSTNDSL

(Seq. ID No. 2)

FIGURE 9C

Amino Acid Sequence of the Chimeric Receptors

Amino acid sequence of the β_2 AR-V2R chimera (Oakley et al.)

MGQPGNGSAFLLAPNRSHAPDHDVTQQRDEVWVVGMGIVMSLIVLAIVFGNVLVITAIK
ERLQTVTNFYFITSACADLVMGAVVPFGAAHILMKMWTFGNFWCEFWTSIDVLCVTASIE
TLCVIAVDYFAITSPFKYQSLLTKNKARVILMVWIVSGLTSFLPIQMHWRATHQEAIN
CYANETCCDFFTQAYAIASSIVSFYVPLVIMVFVYSRVFQEAQRQLQKIDKSEGRFHVQN
LSQVEQDGRGTGHGLRRSSKFCLKEHKALKTLGIIMGTFTLCWLPFFIVNIVHVIQDNLIRK
EVYILLNWIGYVNSGFNPLIYCRSPDFRIAFQELL**CARGRTPPSLGPQDESCTTASSSLAK**
DTSS

(Seq. ID No. 3)

*shown in bold are the amino acids that were moved to the β_2 AR to increase its affinity for arrestin.

REPLACEMENT SHEET

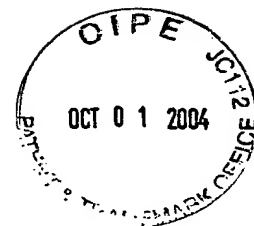


FIGURE 10A

Amino acid sequence of the MOR-V2R chimera expressed from the pEArrB-1/MOR vector

MDSSTGPGNTSDCSDPLAQASCSPAPGSWLNLSHVDGNQSDPCGLNRTGLG
GNDSLCPQTGSPSMVTAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTA
TNIYIFNLALADALATSTLPFQSVNYLMGTWPFGTILCKIVISIDYYNMFT
SIFTLCTMSVDRYIAVCHPVKALDFRTPRNAKIVNVCNWILSSAIGLPVMF
MATTKYRQGSIDCTLTFSSHPTWYWENLLKICVFIFAFIMPILIIITVCYGLM
ILRLKSVRMLSGSKEKDRNLRRITRMVLVVAVFIVCWTPIHIVYIIKALI
TIPETTFQTVSWHFCIALGYTNSCLNPVLYAFLDENFKRCFREFCAAARGR
TPPSLGPQDESCTTASSSLAKDTSS

(Seq. ID No. 4)

FIGURE 10B

Amino acid sequence of the D1AR-V2R chimera expressed from the pEArrB-1/D1AR vector

MAPNTSTMDEAGLPAERDFSFRILTACFLSLLILSTLLGNTLVCAAVIRFR
HLRSKVTNFFVISLAVSDLLVAVLVMPWKAVAEIAGFWPFGSFCNIWVAFD
IMCSTASILNLCVISVDRYWAISSPFQYERKMTPKAAFILISVAWTL SVLI
SFIPVQLSWHKAKPTWPLDGNFTSLEDTEDDNCDTRL SRTYAISSSLISFY
IPVAIMIVTYTTSIYRIAQKQIRRI SALERA AVHAKNCQTTAGNGNPVECAQ
SESSFKMSFKRETKVLKTL SVIMGVFVCCWLPFFISNCMV PFCGSEETQPF
CIDSITFDVFVWFGWANSSLNPIIYAFNADFQKAFSTLLGCYRLCAAARGR
TPPSLGPQDESCTTASSSLAKDTSS

(Seq. ID No. 5)

REPLACEMENT SHEET

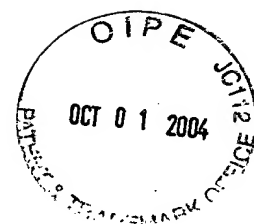


FIGURE 10C

Amino acid sequence of the 5HT1AR-V2R chimera expressed from the pEArrB-1/5HT1AR vector

MDVLSPGQGNNNTTSPAPFETGGNTTGISDVTVSYQVITSLLLGTLI FCAV
LGNACVVAIALERSLQNVANYLIGSLAVTDLMSVSVLVLPMALYQVLNKG
TLGQVTCDLFIALDVLCTSSILHLCAIALDRYWAITDPIDYVNRKTPRRA
AALISLTWLIGFLISIPPMLGWRTPEDRSDPDACTISKDHGYTIYSTFGAF
YIPLLLMLVLYGRIFRAARFRIRKTVKKVEKTGADTRHGASAPQPKSVN
GESGSRNWRLGVESKAGGALCANGAVRQGDDGAALVIEVHRVGNSKEHLP
LPSEAGPTPCAPASFERKNERNAEAKRKMALARERKTVKTLGIIMGTFILC
WLPFFIVALVLPFCESSCHMPTLLGAI
INWLGYSNSLLNPVIYAYFNKDFQNAFKKI IKCNFCAAARGRTPPSLGPQD
ESCTTASSSLAKDTSS

(Seq. ID No. 6)

FIGURE 10D

Amino acid sequence of the β 3AR-V2R chimera expressed from the pEArrB-1/ β 3AR vector

MAPWPHENSSLAPWPDLPNTANTSGLPVPWEAALAGALLALAVLAT
VGGNLLVIVAIANTPRLQTMNTNFVTSLAAADLVMGLLVVPPAATLALTGH
WPLGATGCELWTSVDVLCVTASIEITLCALAVDRYLAVTNPLRYGALVTKRC
ARTAVVLVWVVSAAVSFAPIMSQWVRVGADAEARCHSNPRCCAFASNMPY
VLLSSSVSFYLPLLVMFLVYARVFVATRQLRLLRGELGRFPPEESPAPS
RSLAPAPVGTCPPEGVPACGRPARLLPLREHRALCTLGLIMGTFTLCWL
PFFLANVLRALGGPSLVPGPAFLALNWLGYSANSAFNPLIYCRSPDFRSAFR
RLLCRCAAARGRTPPSLGPQDESCTTASSSLAKDTSS

(Seq. ID No. 7)

FIGURE 10E

Amino acid sequence of the Edg1R-V2R chimera expressed from the pEArrB-1/Edg1R vector

MGPTSVPLVKAHRSSVSDYVNYDIIVRHNYTGKLNISADKENS IKLTSVV
FILICCFIILENIFVLLTIWKTKKFHRPMYYFIGNLALSDLLAGVAYTANL
LLSGATTYKLTPAQWFLREGSMFVALSASFSLAIAIERYITMLKMKLHN
GSNNFRLFLLISACWVISLILGGLPIMGWNCISALSSCSTVLPLYHKHYIL
FCTTVFTLLLLSIVILYCRIYSLVRTRSRLTFRKNISKASRSSEKSLALL
KTVIIVLSVFIACWAPLFI LLLLDVGCKVKTC DILFRAEYFLVLAVLNSGT
NPIIYTLTNKEMRRAFIRIMSCCKCAAARGRTPPSLGPQDESCTTASSSLA
KDTSS

(Seq. ID No. 8)



REPLACEMENT SHEET

FIGURE 11A

Nucleotide sequence of the β 2AR-V2R chimera

atggggcaaccggaacggcagcgccttcttgctggcaccatagaagccatgcgccggacc
acgacgtcacgcagcaaagggacgaggtgtgggtgggcatgggcatcgatgtctctcat
cgtcctggccatcgtgtttggcaatgtgctggatcacagccattgccaaagttcgagcgtctg
cagacggtcaccaactacttcatcacttactggcctgtgctgatctggatgggcctggcag
tggtgccctttggggccgccatattcttatgaaaatgtggacttttggcaacttctggtgoga
gttttggacttccattgatgtgctgtgctcacggccagcattgagaccctgtgctgatcgca
gtggatcgctactttgccattacttcaccttcaagtagcagcctgctgaccaagaataagg
cccgggtgatcattctgatgggtgtggattgtgtcaggccttacctccttcttgccattcagat
gcactggtacggggccaccaccaggaagccatcaactgctatgccaatgagacctgctgtgac
ttcttcacgaaccaagcctatgccattgocctcttccatcgtgtccttctacgttcccctgggtga
tcatgggtcttcgtctactccagggtctttcaggaggccaaaaggcagctccagaagattgacaa
atctgagggccgcttccatgtccagaaccttagccagggtggagcaggatgggcggacggggcat
ggactccgcagatcttccaagttctgcttgaaggagcacaagccctcaagacgttaggcattca
tcatgggcactttcacccctctgctggctgcccttcttcatcgtaacattgtgcatgtgatcca
ggataacctcatccgtaaggaagtttacatcctcctaaattggataggctatgtcaattctgggt
ttcaatccccttatctactgcccggagcccagatttcaggattgccttcaggagcttctgtgcg
cccggggacgcacccaccagcctgggtccccaagatgagtcctgcaccaccgccagctcctc
cctggccaaggacacttcatcgtga

(SEQ ID No. 9)

FIGURE 11B

Nucleotide sequence of the MOR-V2R chimera

atggacagcagcacccggccaggaacaccagcgactgctcagaccccttagctcaggcaagtt
gctccccagcacctggctcctggctcaacttgtcccacgttgatggcaaccagtcgatccatg
cggctctgaaccgcaccgggcttggcggaacgacagcctgtgccctcagaccggcagcccttcc
atgggtcacagccattaccatcatggccctctactctatcgtgtgtgtagtgggcctcttcggaa
acttcctgggtcatgtatgtgattgtgaagatacaccaaaaatgaagactgccaccaacatctacat
tttcaaccttgctctggcagacgccttagcgaccagtagactgccctttcagagtgtcaactac
ctgatgggaacatggcccttcggaaccatcctctgcaagatcgtgatctcaatagattactaca
acatgttcaccagcatattcaccctctgcaccatgagcgtggaccgctacattgctgtctgcca
cccagtcaaaagccctggatttcctgtaccccccgaaatgccaaaatcgtcaacgtctgcaactgg
atcctctcttctgccatcggctctgctgtgaatgttcatggcaaccacaaaatacaggcaggggt
ccatagattgcaccctcacgttctcccacccaacctggtagtgggagaacctgctcaaaatctg
tgtctttatcttcgctttcatcatgcgatcctcatcatcactgtgtgttacggcctgatgatc
ttacgactcaagagcgttcgcatgctatcgggctccaaagaaaaggacaggaatctgcgcagga
tcaccoggatgggtgctgggtcgtggctgtatttatcgtctgctggacccccatccacatcta
cgtcatcatcaaagcgtgatcacgattccagaaaccacatttcagaccgtttcctggcacttc
tgcattgctttgggttacacgaacagctgcctgaatccagttctttacgccttctggatgaaa
acttcaagcgtatgcttcagagagttctgcgcggccgcacggggacgcacccaccagcctggg
tccccaagatgagtcctgcaccaccgccagctcctccttggccaaggacacttcatcgtga

(SEQ ID No. 10)

REPLACEMENT SHEET



FIGURE 11C

Nucleotide sequence of the D1AR-V2R chimera

atggctcctaacttctaccatggatgagggcgggctgccagcggagagggatttctcctttc
gcacctcacggcctgtttcctgtcactgctcactcctgtccactcctcctgggcaataacccttgt
ctgtgcggccgtcatccggtttcgacacctgaggtccaaggtgaccaacttctttgtcatctct
ttagctgtgtcagatctcttgggtggctgtcctgggtcatgccctggaaagctgtggcggagattg
ctggcttttggccctttgggtccttttgtaacatctgggttagcctttgacatcatgtgctctac
ggcgtccattctgaacctctgcgtgatcagcgtggacaggtactgggctatctccagccctttc
cagtatgagaggaagatgaccccaagcagccttcactcctgattagcgtagcatggactctgt
ctgtccttatatccttcaccccagtaacagctggcacaaggcaaagcccacatggccctt
ggatggcaattttacctccctggaggacaccgaggatgacaactgtgacacaaggttgagcagg
acgtatgccatttcactcgtccctcatcagcttttacatcccgtagccattatgatcgtcacct
acaccagtatctacaggattgccagaagcaaaccggcgcatctcagccttgagagggcagca
gtccatgccagaattgccagaccaccgaggttaacgggaaccccgtcgaatgcgccagctctg
aaagttcctttaagatgtccttcaagagggagacgaaagtcttaagacgctgtctgtgatcat
gggggtgtttgtgtgctgctggctccctttctcactctcgaactgtatgggtgcccttctgtggc
tctgaggagaccagccattctgcacgattccatcaccttcgatgtgtttgtgtgggttgggt
gggcgaattcttcctgaacccattatttatgcttttaatgctgacttcagaaggcgttctc
aacctcttaggatgctacagactctgcgcggcgacggggacgcaccccccagcctgggt
ccccaagatgagtcctgcaccaccgcccagctcctccctggccaaggacacttcactgtga
(SEQ ID No. 11)

FIGURE 11D

Nucleotide sequence of the 5HT1AR-V2R chimera

atggatgtgctcagccctggtcagggcaacaacaccacatcaccaccggctccctttgagaccg
gcggcaacactactggtatctccgacgtgacgtcagctaccaagtgatcacctctctgctgct
gggcacgctcatcttctgcgcgggtgctgggcaatgcgtgcgtgggtggctgccatcgccttgag
cgctccctgcagaacgtggccaattatcttattggctctttggcggtcacccagctcatgggtgt
cgggtgttggtgctgcccatggcgcgctgtatcaggtgctcaacaagtggacactgggcccaggt
aacctgcgacctgttcactcgcctcgacgtgctgtgctgcacctcatccatcttgcacctgtgc
gccatcgcgctggacaggtactgggcccacacggaccccatcgactacgtgaacaagaggacgc
ccggcgcgccgctgcgctcatctcgtcacttggttattggcttctcatctctatcccgcc
catgctgggctggcgacccccggaagaccgctcggaccccgacgcatgcaccattagcaaggat
catggctacactatctattccacctttggagctttctacatcccgtgctgctcatgctgggttc
tctatgggcgcataattccgagctgcgcgcttccgcacccgcaagacgggtcaaaaagggtggagaa
gaccggagcggacaccgcctatggagcatctcccgcgcccgagcccaagaagagtgtgaatgga
gagtcggggagcaggaactggaggctgggcgtggagagcaaggctgggggtgctctgtgcgcca
atggcgcggtgaggcaaggtgacgatggcgccgcccctggaggtgatcgaggtgcaccgagtggt
caactccaaagagcacttgctctgcccagcagggctggctcctacccttgtgccccgcctct
ttcgagaggaaaaatgagcgcaacgcgagggcgaagcgcaagatggccctggcccagagagga
agacagtgaagacgctgggcatcatcatgggcaaccttcactcctctgctggctgccttcttcat
cgtggctcttgttctgccccttctgcgagagcagctgccacatgccaccctgttggggcgccata
atcaattggctgggtactccaactctctgcttaaccccgctcatttacgcatacttcaacaagg
actttcaaaacgcgtttaagaagatcattaagtgttaacttctgcgcggcgacggggacgcac
cccaccagcctgggtccccaagatgagtcctgcaccaccgcccagctcctccctggccaaggac
acttcactgtga
(SEQ ID No. 12)



REPLACEMENT SHEET

FIGURE 11E

Nucleotide sequence of the β 3AR-V2R chimera

atgggtccgtggcctcacgagaacagctctcttgccccatggccggacctccccaccctggcgc
ccaataaccgccaacaccagtgggctgccaggggttcogtgggaggcgccctagccggggccct
gctggcgctggcggtgctggccaccgtgggaggcaacctgctgggtcatcgtggccatcgctgg
actccgagactccagaccatgaccaacgtgttcgtgacttcgctggccgcagccgacctggtga
tgggactcctgggtggtgccgcccggcgccaccttggcgctgactggccactggccggttgggogc
cactggctgcgagctgtggacctcgggtggacgtgctgtgtgtgaccgccagcatcgaaacctg
tgcgccctggccgtggaccgctacctggctgtgaccaaccgctgctgttacggcgcaactggtca
ccaagcgtgcgcccggacagctgtggtcctgggtgtgggtcgtgtcgcccgcggtgtcgtttgc
gccccatcatgagccagtgggtggcgcgtagggggccgacgcccagggcgagcgctgccactccaac
ccgcgctgctgtgccttcgcctccaacatgccctacgtgctgctgtcctcctccgtctccttct
accttctcttctcgtgatgctcttcgtctacgcgcgggttttcgtgggtggctacgcgccagct
gcgcttgctgcgcggggagctgggcccgtttccgcccagaggagtctccgcccggcgccgtcgcg
tctctggccccggccccgggtggggacgtgctgctccgcccgaaggggtgcccgcctgcccgcggc
ggccccgcgcgcctcctgcctctccgggaacaccggggccctgtgcaccttgggtctcatcatggg
caccttcactctctgctgggtgccccttcttctggccaacgtgctgcgcgccctggggggcccc
tctctagtcccgggccccggcttcttctgcccgaactggctaggttatgccaatctgccttca
accgctcatctactgccgcagcccggactttcgcagcgccctccgcccgtcttctgtgccgctg
cgcgggcgcaagggggacgcacccccaccagcctgggtccccaagatgagtcctgcaccaccgcca
gtcctccttgcccaaggacacttcatcgtga

(SEQ ID No. 13)

FIGURE 11F

Nucleotide sequence of the Edg1-V2R chimera

atggggcccaccagcgtcccgtggtcaaggcccaccgcagctcgggtctctgactacgtcaact
atgatatcatcgtccggcattacaactacacgggaaagctgaatatcagcgcgggacaaggagaa
cagcattaaactgacctcgggtggtgttcattctcatctgctgctttatcatcctgggagaacatc
tttgtcttgctgacctttggaaaaccaagaaattccaccgacctatgtactattttatggca
atctggccctctcagacctgttggcaggagtagcctacacagctaacctgctcttgtctggggc
caccacctacaagctcactcccgcgccagtgggttctgcccgaaggagtagtgttgggtggccctg
tcagcctccgtgttcagtctcctcgccatcgccattgagcgctatatcacaatgctgaaaatga
aactccacaacgggagcaataaacttcgcctcttctgctaatcagcgctgctgggtcatctc
cctcatcctgggtggcctgctatcatgggctgggaactgcatcagtgcgctgtccagctgctcc
accgtgctgcccgtctaccacaagcactatcctcttctgcaccacgggtcttcaactctgcttc
tgctctccatcgtcatctgtactgcagaatctactccttgggtcaggactcggagccgcgcct
gacgttccgcaagaacatttccaaggccagccgcagctctgagaagtgcgtggcgctgctcaag
accgtaattatcgtcctgagcgtcttcatcgccgtgctgggcaaccgctcttcatcctgctcctgc
tggtatgtgggtgcaagggtgaagacctgtgacatcctcttcagagcggagtagtctcctgggtgt
agctgtgctcaactccggcaccaccccatcatttacactctgaccaacaaggagatgcgtcgg
gccttcatccggatcatgtcctgctgcaagtgcgcggccgcacggggacgcacccccaccagcc
tgggtccccaagatgagtcctgcaccaccgcccagctcctccttgcccaaggacacttcatcgtg

a

(SEQ ID No. 14)